

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (Currently Amended) A method of forming a tunable active agent delivery system having a target diffusivity, the method comprising:

providing a hydrophobic active agent having a solubility parameter and a molecular weight of no greater than about 1200 g/mol; and

~~providing combining the hydrophobic active agent with~~ a miscible polymer blend that is capable of controlling delivery of the active agent, comprising and comprises:

providing a first miscible polymer having a solubility parameter, ~~and~~

providing a second polymer selected to be miscible with the first polymer and having a solubility parameter, and

combining the first miscible polymer and the second polymer to form the miscible polymer blend;

wherein:

the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of the polymers is no greater than about  $3 \text{ } 5 \text{ J}^{1/2}/\text{cm}^{3/2}$ ;

at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity;

the molar average solubility parameter of the blend is no greater than  $25 \text{ J}^{1/2}/\text{cm}^{3/2}$ ; and

the swellability of the blend is no greater than 10% by volume;

and further wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polyvinyl homopolymer or copolymer selected from the group consisting of a polyvinyl alkylate homopolymer or copolymer, a polyvinyl alkyl ether homopolymer or copolymer, a polyvinyl acetal homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof; or

the miscible polymer blend comprises a poly(ethylene-co-(meth)acrylate) and a second miscible polymer not including poly(ethylene vinyl acetate); wherein the second miscible polymer is selected from the group consisting of a poly(vinyl alkylate) homopolymer or copolymer, a poly(vinyl alkyl ether) homopolymer or copolymer, a poly(vinyl acetal) homopolymer or copolymer, a poly(alkyl and/or aryl methacrylate) homopolymer or copolymer, a poly(alkyl and/or aryl acrylate) homopolymer or copolymer, and combinations thereof.

2. (Previously Presented) The method of claim 1 wherein:

the miscible polymer blend does not include a blend of a hydrophobic cellulose derivative and a polyurethane or a polyvinyl pyrrolidone; and/or

the miscible polymer blend does not include a blend of a polyalkyl methacrylate and a polyethylene-co-vinyl acetate.

3. (Previously Presented) The method of claim 1 wherein the difference between at least one Tg of at least two of the polymers corresponds to a range of diffusivities that includes the target diffusivity.

4. (Previously Presented) The method of claim 1 wherein the active agent is incorporated within the miscible polymer blend.

5. (Previously Presented) The method of claim 1 wherein the miscible polymer blend initially provides a barrier for permeation of the active agent.

6. (Previously Presented) The method of claim 1 wherein the active agent is incorporated within an inner matrix.

7. (Previously Presented) The method of claim 1 wherein the miscible polymer blend includes at least one hydrophobic polymer.

8. (Previously Presented) The method of claim 1 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $5 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

9. (Currently Amended) The method of claim 8 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of each of at least one ~~two~~ of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

10. (Currently Amended) A method of forming a tunable active agent delivery system having a target diffusivity, the method comprising:

providing a hydrophilic active agent having a solubility parameter and a molecular weight of no greater than about 1200 g/mol; and

providing combining the hydrophilic active agent with a miscible polymer blend that is capable of controlling delivery of the active agent, comprising and comprises:

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

providing a first miscible polymer having a solubility parameter, and  
providing a second polymer selected to be miscible with the first polymer and  
having a solubility parameter, and  
combining the first miscible polymer and the second polymer to form the miscible  
polymer blend;

wherein:

the difference between the solubility parameter of the active agent and at least one  
solubility parameter of at least one of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ ,  
and the difference between at least one solubility parameter of each of at least two  
polymers is no greater than about  $3 \pm \text{J}^{1/2}/\text{cm}^{3/2}$ ;

at least one polymer has an active agent diffusivity higher than the target  
diffusivity and at least one polymer has an active agent diffusivity lower than the target  
diffusivity;

the molar average solubility parameter of the blend is greater than  $25 \text{ J}^{1/2}/\text{cm}^{3/2}$ ;  
and

the swellability of the blend is no greater than 10% by volume;  
and further wherein:

the miscible polymer blend comprises miscible polymers selected from the  
group consisting of polyacrylonitriles, cyanoacrylates, methacrylonitriles,  
hydrophilic cellulose, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and at least one  
miscible hydrophilic polymer selected from the group consisting of a  
polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a  
polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl  
pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl  
pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic

cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; or

the miscible polymer blend comprises two hydrophobic polyurethanes as a cap coat in a reservoir system.

11. (Previously Presented) The method of claim 10 wherein the miscible polymer blend does not include both a hydrophobic cellulose derivative and a polyvinyl pyrrolidone.

12. (Previously Presented) The method of claim 10 wherein the difference between at least one Tg of at least two of the polymers corresponds to a range of diffusivities that includes the target diffusivity.

13. (Previously Presented) The method of claim 10 wherein the active agent is incorporated within the miscible polymer blend.

14. (Previously Presented) The method of claim 10 wherein the miscible polymer blend initially provides a barrier for permeation of the active agent.

15. (Previously Presented) The method of claim 14 wherein the active agent is incorporated within an inner matrix.

16. (Previously Presented) The method of claim 10 wherein the miscible polymer blend includes at least one hydrophilic polymer.

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

17. (Previously Presented) The method of claim 10 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $5 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

18. (Currently Amended) The method of claim ~~17~~ 10 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of each of at least one ~~two~~ of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

19. (Canceled)

20. (Currently Amended) A method of forming a tunable active agent delivery system having a target diffusivity, the method comprising:

providing a hydrophobic active agent having a solubility parameter and a molecular weight of greater than about 1200 g/mol; and

providing combining the hydrophobic active agent with a miscible polymer blend that is capable of controlling delivery of the active agent, comprising and comprises:

providing a first miscible polymer having a solubility parameter, and

providing a second polymer selected to be miscible with the first polymer and having a solubility parameter, and

combining the first miscible polymer and the second polymer to form the miscible polymer blend;

wherein:

the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of at least two polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ ;

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity;

the molar average solubility parameter of the blend is no greater than  $25 \text{ J}^{1/2}/\text{cm}^{3/2}$ ;

and

the swellability of the blend is greater than 10% by volume;

and further wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polymer selected from the group consisting of polyethylene, polypropylene, polyisobutylene, polystyrene, poly(vinyl chloride), poly(vinyl bromide), poly(vinylidene chloride), poly(tetrafluoroethylene), poly(chloro trifluoroethylene), poly(vinyl alcohol), poly(vinyl acetate), poly(vinyl propionate), poly(methyl acrylate), poly(ethyl acrylate), poly(propyl acrylate), poly(butyl acrylate), poly(isobutyl acrylate), poly(2,2,3,3,4,4,4-heptafluorobutyl acrylate), poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(tert-butyl methacrylate), poly(benzyl methacrylate), poly(ethoxyethyl methacrylate), polyacrylonitrile, polymethacrylonitrile, poly(alpha-cyanomethyl acrylate), polybutadiene, polyisoprene, polychloroprene, polyformaldehyde, poly(tetramethylene oxide), poly(propylene oxide), polyepichlorohydrin, poly(ethylene sulphide), poly(styrene sulphide), poly(ethylene terephthalate), poly(8-aminocaprylic acid), poly(hexamethylene adipamide), polyurethane hard segment (MDI + BDO), poly(bisphenyl A carbonate), cellulose acetate butyrate, phenoxy, poly(vinyl pyrrolidone), poly(vinyl pyrrolidone)-co-poly(vinyl acetate), poly(ethylene oxide), and combinations thereof.

21. (Previously Presented) The method of claim 20 wherein:  
the miscible polymer blend does not include a blend of a hydrophobic cellulose derivative and a polyurethane or a polyvinyl pyrrolidone; and/or  
the miscible polymer blend does not include a blend of a polyalkyl methacrylate and a polyethylene-co-vinyl acetate.
22. (Previously Presented) The method of claim 20 wherein the difference between the swellabilities of at least two of the polymers corresponds to a range of diffusivities that includes the target diffusivity.
23. (Previously Presented) The method of claim 20 wherein the active agent is incorporated within the miscible polymer blend.
24. (Previously Presented) The method of claim 20 wherein the miscible polymer blend initially provides a barrier for permeation of the active agent.
25. (Previously Presented) The method of claim 24 wherein the active agent is incorporated within an inner matrix.
26. (Previously Presented) The method of claim 20 wherein the second polymer of the miscible polymer blend is a hydrophobic polymer.
27. (Previously Presented) The method of claim 26 wherein the miscible polymer blend includes a second polymer that is hydrophilic.



Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

28. (Previously Presented) The method of claim 27 wherein the hydrophilic polymer is a hydrophilic polyurethane.

29. (Previously Presented) The method of claim 20 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $5 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

30. (Currently Amended) The method of claim ~~29~~ 20 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of ~~each of~~ at least one ~~two~~ of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

31. (Previously Presented) The method of claim 20 wherein the active agent is not heparin.

32. (Currently Amended) A method of forming a tunable active agent delivery system having a target diffusivity, the method comprising:

providing a hydrophilic active agent having a solubility parameter and a molecular weight of greater than about 1200 g/mol; and

~~providing combining the hydrophilic active agent with a miscible polymer blend that is capable of controlling delivery of the active agent, comprising and comprises:~~

providing a first miscible polymer having a solubility parameter, and

providing a second polymer selected to be miscible with the first polymer and

having a solubility parameter, and

combining the first miscible polymer and the second polymer to form a miscible polymer blend;

wherein:

the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of at least two polymers is no greater than about  $3 \pm \text{J}^{1/2}/\text{cm}^{3/2}$ ;

at least one polymer has an active agent diffusivity higher than the target diffusivity and at least one polymer has an active agent diffusivity lower than the target diffusivity;

the molar average solubility parameter of the blend is greater than  $25 \text{ J}^{1/2}/\text{cm}^{3/2}$ ;  
and

the swellability of the blend is greater than 10% by volume;  
and further wherein:

the miscible polymer blend comprises at least one hydrophilic polymer and a second miscible polymer that is hydrophilic or hydrophobic; wherein the hydrophilic polymer is selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; and the hydrophobic polymer is selected from the group consisting of a polyurethane, a polycarbonate, a polysulfone, a polyphenylene oxide osied, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a polyvinyl alkylate, a polyvinyl alkyl ether, a polyvinyl acetal, a hydrophobic cellulose derivative, and combinations thereof.

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

33. (Previously Presented) The method of claim 32 wherein the miscible polymer blend does not include both a hydrophobic cellulose derivative and a polyvinyl pyrrolidone.

34. (Previously Presented) The method of claim 32 wherein the difference between the swellabilities of at least two of the polymers corresponds to a range of diffusivities that includes the target diffusivity.

35. (Previously Presented) The method of claim 32 wherein the active agent is incorporated within the miscible polymer blend.

36. (Previously Presented) The method of claim 32 wherein the miscible polymer blend initially provides a barrier for permeation of the active agent.

37. (Previously Presented) The method of claim 36 wherein the active agent is incorporated within an inner matrix.

38. (Previously Presented) The method of claim 32 wherein the miscible polymer blend includes at least one hydrophilic polymer.

39. (Previously Presented) The method of claim 38 wherein one polymer is a hydrophilic polyurethane.

40. (Previously Presented) The method of claim 38 wherein the miscible polymer blend includes a second polymer that is hydrophobic.

41. (Previously Presented) The method of claim 32 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of at least one of the polymers is no greater than about  $5 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

42. (Currently Amended) The method of claim ~~41~~ 32 wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of ~~each of~~ at least one ~~two~~ of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ .

43. (Previously Presented) The method of claim 32 wherein the active agent is not heparin.

44. (Previously Presented) A method of making a medical device comprising;  
providing a medical device comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 1 to at least a portion of the surface.

45. (Currently Amended) The method of claim 44, wherein the medical device is selected from the group consisting of a stent, stent graft, anastomotic connector, lead, needle, guide wire, catheter, sensor, surgical instrument, angioplasty balloon, wound drain, shunt, tubing, urethral insert, pellet, implant, blood oxygenator, pump, vascular graft, valve, pacemaker, orthopedic device, replacement device for nucleus pulposus, and intraocular lens ~~lense~~.

46. (Previously Presented) A method of making a medical device comprising;  
providing a medical device comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 10 to at least a portion of the surface.

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

47. (Currently Amended) The method of claim 46, wherein the medical device is selected from the group consisting of a stent, stent graft, anastomotic connector, lead, needle, guide wire, catheter, sensor, surgical instrument, angioplasty balloon, wound drain, shunt, tubing, urethral insert, pellet, implant, blood oxygenator, pump, vascular graft, valve, pacemaker, orthopedic device, replacement device for nucleus pulposus, and intraocular lens ~~lense~~.

48. (Previously Presented) A method of making a medical device comprising;  
providing a medical device comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 20 to at least a portion of the surface.

49. (Currently Amended) The method of claim 48, wherein the medical device is selected from the group consisting of a stent, stent graft, anastomotic connector, lead, needle, guide wire, catheter, sensor, surgical instrument, angioplasty balloon, wound drain, shunt, tubing, urethral insert, pellet, implant, blood oxygenator, pump, vascular graft, valve, pacemaker, orthopedic device, replacement device for nucleus pulposus, and intraocular lens ~~lense~~.

50. (Previously Presented) A method of making a medical device comprising;  
providing a medical device comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 32 to at least a portion of the surface.

51. (Currently Amended) The method of claim 50, wherein the medical device is selected from the group consisting of a stent, stent graft, anastomotic connector, lead, needle, guide wire, catheter, sensor, surgical instrument, angioplasty balloon, wound drain, shunt, tubing, urethral

insert, pellet, implant, blood oxygenator, pump, vascular graft, valve, pacemaker, orthopedic device, replacement device for nucleus pulposus, and intraocular lens lense.

52. (Previously Presented) A method of making a stent comprising;  
providing a stent comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 1 to at least a portion of the surface.
53. (Previously Presented) A method of making a stent comprising;  
providing a stent comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 10 to at least a portion of the surface.
54. (Previously Presented) A method of making a stent comprising;  
providing a stent comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 20 to at least a portion of the surface.
55. (Previously Presented) A method of making a stent comprising;  
providing a stent comprising a surface; and  
adhering an active agent delivery system formed by the method of claim 32 to at least a portion of the surface.
56. (Currently Amended) A method of designing an active agent delivery system for delivering an active agent over a preselected dissolution time (t) through a preselected critical

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

dimension (x) of a miscible polymer blend that controls delivery of the active agent, the method comprising:

providing an active agent having a solubility parameter and a molecular weight no greater than about 1200 g/mol;

providing a first miscible polymer having a solubility parameter;

selecting a second polymer to be miscible with the first polymer and having a solubility parameter, wherein:

the difference between the solubility parameter of the active agent and at least one solubility parameter of each of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of the polymers is no greater than about  $3 \pm \text{J}^{1/2}/\text{cm}^{3/2}$ ;

the difference between at least one Tg of each of the polymers is sufficient to include the target diffusivity;

~~combining the polymers to form a miscible polymer blend; and~~

combining the first miscible polymer ~~blend~~ with the second polymer ~~active agent~~ to form an active agent delivery system comprising the miscible polymer blend and having the preselected dissolution time through a preselected critical dimension of the miscible polymer blend;

wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polyvinyl homopolymer or copolymer selected from the group consisting of a polyvinyl alkylate homopolymer or copolymer, a polyvinyl alkyl ether homopolymer or copolymer, a polyvinyl acetal homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof; or

the miscible polymer blend comprises a poly(ethylene-co-(meth)acrylate) and a second miscible polymer not including poly(ethylene vinyl acetate); wherein the second miscible polymer is selected from the group consisting of a poly(vinyl alkylate) homopolymer or copolymer, a poly(vinyl alkyl ether) homopolymer or copolymer, a poly(vinyl acetal) homopolymer or copolymer, a poly(alkyl and/or aryl methacrylate) homopolymer or copolymer, a poly(alkyl and/or aryl acrylate) homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises miscible polymers selected from the group consisting of polyacrylonitriles, cyanoacrylates, methacrylonitriles, hydrophilic cellulose, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and at least one miscible hydrophilic polymer selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; or

the miscible polymer blend comprises two hydrophobic polyurethanes as a cap coat in a reservoir system.



57. (Original) The method of claim 56 wherein the active agent is incorporated within the miscible polymer blend.

58. (Original) The method of claim 56 wherein miscible polymer blend initially provides a barrier for permeation of the active agent.

59. (Original) The method of claim 56 wherein the active agent is incorporated within an inner matrix.

60. (Original) The method of claim 56 wherein the active agent is hydrophobic.

61. (Previously Presented) The method of claim 56 wherein the active agent is hydrophilic.

62. (Previously Presented) The method of claim 56 wherein:

the miscible polymer blend does not include a blend of a hydrophobic cellulose derivative and a polyurethane or a polyvinyl pyrrolidone; and/or

the miscible polymer blend does not include a blend of a polyalkyl methacrylate and a polyethylene-co-vinyl acetate.

63. (Currently Amended) A method of designing an active agent delivery system for delivering an active agent over a preselected dissolution time (t) through a preselected critical dimension (x) of a miscible polymer blend that controls delivery of the active agent, the method comprising:

providing an active agent having a solubility parameter and a molecular weight greater than about 1200 g/mol;

providing a first miscible polymer having a solubility parameter;

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

selecting a second polymer to be miscible with the first polymer and having a solubility parameter, wherein:

the difference between the solubility parameter of the active agent and at least one solubility parameter of each of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of the polymers is no greater than about  $3 \pm \text{J}^{1/2}/\text{cm}^{3/2}$ ;

the difference between the swellabilities of the polymers is sufficient to include the target diffusivity;

~~combining the polymers to form a miscible polymer blend;~~ and

combining the first miscible polymer blend with the second polymer active agent to form an active agent delivery system comprising a miscible polymer blend and having the preselected dissolution time through a preselected critical dimension of the miscible polymer blend;

wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and a second polymer selected from the group consisting of polyethylene, polypropylene, polyisobutylene, polystyrene, poly(vinyl chloride), poly(vinyl bromide), poly(vinylidene chloride), poly(tetrafluoroethylene), poly(chloro trifluoroethylene), poly(vinyl alcohol), poly(vinyl acetate), poly(vinyl propionate), poly(methyl acrylate), poly(ethyl acrylate), poly(propyl acrylate), poly(butyl acrylate), poly(isobutyl acrylate), poly(2,2,3,3,4,4,4-heptafluorobutyl acrylate), poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(tert-butyl methacrylate), poly(benzyl methacrylate), poly(ethoxyethyl methacrylate), polyacrylonitrile, polymethacrylonitrile, poly(alpha-cyanomethyl acrylate), polybutadiene, polyisoprene, polychloroprene, polyformaldehyde, poly(tetramethylene oxide), poly(propylene oxide), polyepichlorohydrin, poly(ethylene sulphide), poly(styrene sulphide), poly(ethylene terephthalate), poly(8-aminocaprylic acid), poly(hexamethylene

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

adipamide), polyurethane hard segment (MDI + BDO), poly(bisphenyl A carbonate), cellulose acetate butyrate, phenoxy, poly(vinyl pyrrolidone), poly(vinyl pyrrolidone)-co-poly(vinyl acetate), poly(ethylene oxide), and combinations thereof; or

the miscible polymer blend comprises at least one hydrophilic polymer and a second miscible polymer that is hydrophilic or hydrophobic; wherein the hydrophilic polymer is selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; and the hydrophobic polymer is selected from the group consisting of a polyurethane, a polycarbonate, a polysulfone, a polyphenylene oxide ~~esied~~, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a polyvinyl alkylate, a polyvinyl alkyl ether, a polyvinyl acetal, a hydrophobic cellulose derivative, and combinations thereof.

64. (Original) The method of claim 63 wherein the active agent is incorporated within the miscible polymer blend.

65. (Original) The method of claim 63 wherein miscible polymer blend initially provides a barrier for permeation of the active agent.

66. (Original) The method of claim 63 wherein the active agent is incorporated within an inner matrix.

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

67. (Original) The method of claim 63 wherein the active agent is hydrophobic.

68. (Original) The method of claim 63 wherein the active agent is hydrophilic.

69. (Original) The method of claim 63 wherein the active agent is not heparin.

70. (Original) The method of claim 63 wherein:

the miscible polymer blend does not include a blend of a hydrophobic cellulose derivative and a polyurethane or a polyvinyl pyrrolidone; and/or

the miscible polymer blend does not include a blend of a polyalkyl methacrylate and a polyethylene-co-vinyl acetate.

71. (Previously Presented) A method for delivering an active agent to a subject, the method comprising:

providing the active agent delivery system formed according to the method of claim 1;  
and

contacting the active agent delivery system with a bodily fluid, organ, or tissue of a subject.

72. (Previously Presented) A method for delivering an active agent to a subject, the method comprising:

providing the active agent delivery system formed according to the method of claim 10;  
and

contacting the active agent delivery system with a bodily fluid, organ, or tissue of a subject.

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

73. (Previously Presented) A method for delivering an active agent to a subject, the method comprising:

providing the active agent delivery system formed according to the method of claim 20;

and

contacting the active agent delivery system with a bodily fluid, organ, or tissue of a subject.

74. (Previously Presented) A method for delivering an active agent to a subject, the method comprising:

providing the active agent delivery system formed according to the method of claim 32;

and

contacting the active agent delivery system with a bodily fluid, organ, or tissue of a subject.

75. (Currently Amended) A method for tuning the delivery of an active agent to a subject, the method comprising:

providing an active agent delivery system comprising an active agent having a molecular weight no greater than about 1200 g/mol and a miscible polymer blend, comprising:

providing a first miscible polymer having a solubility parameter;

selecting a second polymer to be miscible with the first polymer and having a solubility parameter;

combining the first polymer and the second polymer to form the a miscible polymer blend that controls the delivery of the active agent; wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of each of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ ; and

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

combining the miscible polymers and the ~~an~~ active agent in amounts sufficient to form the active agent delivery system comprising the a miscible polymer blend capable of delivering the ~~an~~ active agent at a predetermined release rate; and

contacting the active agent delivery system with a bodily fluid, organ, or tissue of a subject to deliver the active agent at the predetermined release rate;

wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polyvinyl homopolymer or copolymer selected from the group consisting of a polyvinyl alkylate homopolymer or copolymer, a polyvinyl alkyl ether homopolymer or copolymer, a polyvinyl acetal homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof; or

the miscible polymer blend comprises a poly(ethylene-co-(meth)acrylate) and a second miscible polymer not including poly(ethylene vinyl acetate); wherein the second miscible polymer is selected from the group consisting of a poly(vinyl alkylate) homopolymer or copolymer, a poly(vinyl alkyl ether) homopolymer or copolymer, a poly(vinyl acetal) homopolymer or copolymer, a poly(alkyl and/or aryl methacrylate) homopolymer or copolymer, a poly(alkyl and/or aryl acrylate) homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises miscible polymers selected from the group consisting of polyacrylonitriles, cyanoacrylates, methacrylonitriles, hydrophilic cellulose, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and at least one miscible hydrophilic polymer selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; or

the miscible polymer blend comprises two hydrophobic polyurethanes as a cap coat in a reservoir system.

76-77. (Canceled)

78. (Currently Amended) A method for tuning the delivery of an active agent to a subject, the method comprising:

providing an active agent delivery system comprising an active agent having a molecular weight greater than about 1200 g/mol and a miscible polymer blend, comprising:

providing a first miscible polymer having a solubility parameter;

selecting a second polymer to be miscible with the first polymer and having a solubility parameter;

combining the first polymer and the second polymer to form the a miscible polymer blend that controls the delivery of the active agent; wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of each of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

at least one solubility parameter of each of the polymers is no greater than about  $3.5 \text{ J}^{1/2}/\text{cm}^{3/2}$ ; and

combining the miscible polymers and ~~the an~~ active agent in amounts sufficient to form the active agent delivery system comprising ~~the a~~ a miscible polymer blend capable of delivering ~~the an~~ active agent at a predetermined release rate; and  
contacting the active agent delivery system with a bodily fluid, organ, or tissue of a subject to deliver the active agent at the predetermined release rate;

wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polymer selected from the group consisting of polyethylene, polypropylene, polyisobutylene, polystyrene, poly(vinyl chloride), poly(vinyl bromide), poly(vinylidene chloride), poly(tetrafluoroethylene), poly(chloro trifluoroethylene), poly(vinyl alcohol), poly(vinyl acetate), poly(vinyl propionate), poly(methyl acrylate), poly(ethyl acrylate), poly(propyl acrylate), poly(butyl acrylate), poly(isobutyl acrylate), poly(2,2,3,3,4,4,4-heptafluorobutyl acrylate), poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(tert-butyl methacrylate), poly(benzyl methacrylate), poly(ethoxyethyl methacrylate), polyacrylonitrile, polymethacrylonitrile, poly(alpha-cyanomethyl acrylate), polybutadiene, polyisoprene, polychloroprene, polyformaldehyde, poly(tetramethylene oxide), poly(propylene oxide), polyepichlorohydrin, poly(ethylene sulphide), poly(styrene sulphide), poly(ethylene terephthalate), poly(8-aminocaprylic acid), poly(hexamethylene adipamide), polyurethane hard segment (MDI + BDO), poly(bisphenyl A carbonate), cellulose acetate butyrate, phenoxy, poly(vinyl pyrrolidone), poly(vinyl pyrrolidone)-co-poly(vinyl acetate), poly(ethylene oxide), and combinations thereof; or

the miscible polymer blend comprises at least one hydrophilic polymer and a second miscible polymer that is hydrophilic or hydrophobic; wherein the hydrophilic



Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

polymer is selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; and the hydrophobic polymer is selected from the group consisting of a polyurethane, a polycarbonate, a polysulfone, a polyphenylene oxide esied, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a polyvinyl alkylate, a polyvinyl alkyl ether, a polyvinyl acetal, a hydrophobic cellulose derivative, and combinations thereof.

79. (New) A method of forming a tunable active agent delivery system comprising:
- providing an active agent;
  - providing a first miscible polymer having a solubility parameter;
  - selecting a second polymer to be miscible with the first polymer to form a miscible polymer blend that controls the delivery of the active agent having a molecular weight of no greater than about 1200 g/mol; wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of each of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ ; and
  - combining the miscible polymers in amounts sufficient to form the miscible polymer blend capable of delivering the active agent at a predetermined release rate; and
  - combining the active agent with the miscible polymer blend such that the miscible polymer blend controls the delivery of the active agent at the predetermined release rate;

wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polyvinyl homopolymer or copolymer selected from the group consisting of a polyvinyl alkylate homopolymer or copolymer, a polyvinyl alkyl ether homopolymer or copolymer, a polyvinyl acetal homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and a second miscible polymer that is not a hydrophobic cellulose ester; wherein the second miscible polymer is selected from the group consisting of a polycarbonate, a polysulfone, a polyurethane, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a poly(vinyl ester), a poly(vinyl ether), a polyacrylate, a poly(methyl acrylate), a polymethacrylate, a poly(methyl methacrylate), and combinations thereof; or

the miscible polymer blend comprises a poly(ethylene-co-(meth)acrylate) and a second miscible polymer not including poly(ethylene vinyl acetate); wherein the second miscible polymer is selected from the group consisting of a poly(vinyl alkylate) homopolymer or copolymer, a poly(vinyl alkyl ether) homopolymer or copolymer, a poly(vinyl acetal) homopolymer or copolymer, a poly(alkyl and/or aryl methacrylate) homopolymer or copolymer, a poly(alkyl and/or aryl acrylate) homopolymer or copolymer, and combinations thereof; or

the miscible polymer blend comprises miscible polymers selected from the group consisting of polyacrylonitriles, cyanoacrylates, methacrylonitriles, hydrophilic cellulose derivatives, and combinations thereof; or

the miscible polymer blend comprises a polyurethane and at least one miscible hydrophilic polymer selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; or

the miscible polymer blend comprises two hydrophobic polyurethanes as a cap coat in a reservoir system.

80. (New) A method of forming a tunable active agent delivery system comprising:

providing an active agent;

providing a first miscible polymer having a solubility parameter;

selecting a second polymer to be miscible with the first polymer to form a miscible polymer blend that controls the delivery of the active agent having a molecular weight of greater than about 1200 g/mol; wherein the difference between the solubility parameter of the active agent and at least one solubility parameter of each of the polymers is no greater than about  $10 \text{ J}^{1/2}/\text{cm}^{3/2}$ , and the difference between at least one solubility parameter of each of the polymers is no greater than about  $3 \text{ J}^{1/2}/\text{cm}^{3/2}$ ; and

combining the first polymer and the second polymer in amounts sufficient to form the miscible polymer blend capable of delivering the active agent at a predetermined release rate; and

combining the active agent with the miscible polymer blend such that the miscible polymer blend controls the delivery of the active agent at the predetermined release rate;

wherein:

the miscible polymer blend comprises at least one hydrophobic cellulose derivative and at least one miscible polymer selected from the group consisting of polyethylene, polypropylene, polyisobutylene, polystyrene, poly(vinyl chloride), poly(vinyl bromide), poly(vinylidene chloride), poly(tetrafluoroethylene), poly(chloro trifluoroethylene), poly(vinyl alcohol), poly(vinyl acetate), poly(vinyl propionate), poly(methyl acrylate), poly(ethyl acrylate), poly(propyl acrylate), poly(butyl acrylate),

Serial No.: 10/640,853

Confirmation No.: 9178

Filed: August 13, 2005

For: ACTIVE AGENT DELIVERY SYSTEMS, MEDICAL DEVICES, AND METHODS

---

poly(isobutyl acrylate), poly(2,2,3,3,4,4,4-heptafluorobutyl acrylate), poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(tert-butyl methacrylate), poly(benzyl methacrylate), poly(ethoxyethyl methacrylate), polyacrylonitrile, polymethacrylonitrile, poly(alpha-cyanomethyl acrylate), polybutadiene, polyisoprene, polychloroprene, polyformaldehyde, poly(tetramethylene oxide), poly(propylene oxide), polyepichlorohydrin, poly(ethylene sulphide), poly(styrene sulphide), poly(ethylene terephthalate), poly(8-aminocaprylic acid), poly(hexamethylene adipamide), polyurethane hard segment (MDI + BDO), poly(bisphenyl A carbonate), cellulose acetate butyrate, phenoxy, poly(vinyl pyrrolidone), poly(vinyl pyrrolidone)-co-poly(vinyl acetate), poly(ethylene oxide), and combinations thereof; or

the miscible polymer blend comprises at least one hydrophilic polymer and a second miscible polymer that is hydrophilic or hydrophobic; wherein the hydrophilic polymer is selected from the group consisting of a polyurethane, a polyvinyl alcohol, a poly(alkylene ether), a polyvinyl pyridine, a polyvinyl pyrrolidone, a polyacrylonitrile, a polyacrylamide, a polyvinyl pyrrolidone/polyvinyl acetate copolymer, a sulfonated polystyrene, a polyvinyl pyrrolidone/polystyrene copolymer, a polysaccharide, a xanthan, a hydrophilic cellulose derivative, a hyaluronic acid, a hydrophilic polyacrylate, a hydrophilic polymethacrylate, a DNA or analog thereof, an RNA or analog thereof, heparin, a chitosan, a polyethylene imine, a polyacrylamide, an amine-containing polymer, and combinations thereof; and the hydrophobic polymer is selected from the group consisting of a polyurethane, a polycarbonate, a polysulfone, a polyphenylene oxide, a polyimide, a polyamide, a polyester, a polyether, a polyketone, a polyepoxide, a styrene-acrylonitrile copolymer, a polyvinyl alkylate, a polyvinyl alkyl ether, a polyvinyl acetal, a hydrophobic cellulose derivative, and combinations thereof.

81. (New) The method of claim 75 wherein the active agent is incorporated within the miscible polymer blend.

82. (New) The method of claim 75 wherein the active agent is incorporated within an inner matrix.

83. (New) The method of claim 78 wherein the active agent is incorporated within the miscible polymer blend.

84. (New) The method of claim 78 wherein the active agent is incorporated within an inner matrix.

85. (New) The method of claim 79 wherein the active agent is incorporated within the miscible polymer blend.

86. (New) The method of claim 79 wherein the active agent is incorporated within an inner matrix.

87. (New) The method of claim 80 wherein the active agent is incorporated within the miscible polymer blend.

88. (New) The method of claim 80 wherein the active agent is incorporated within an inner matrix.